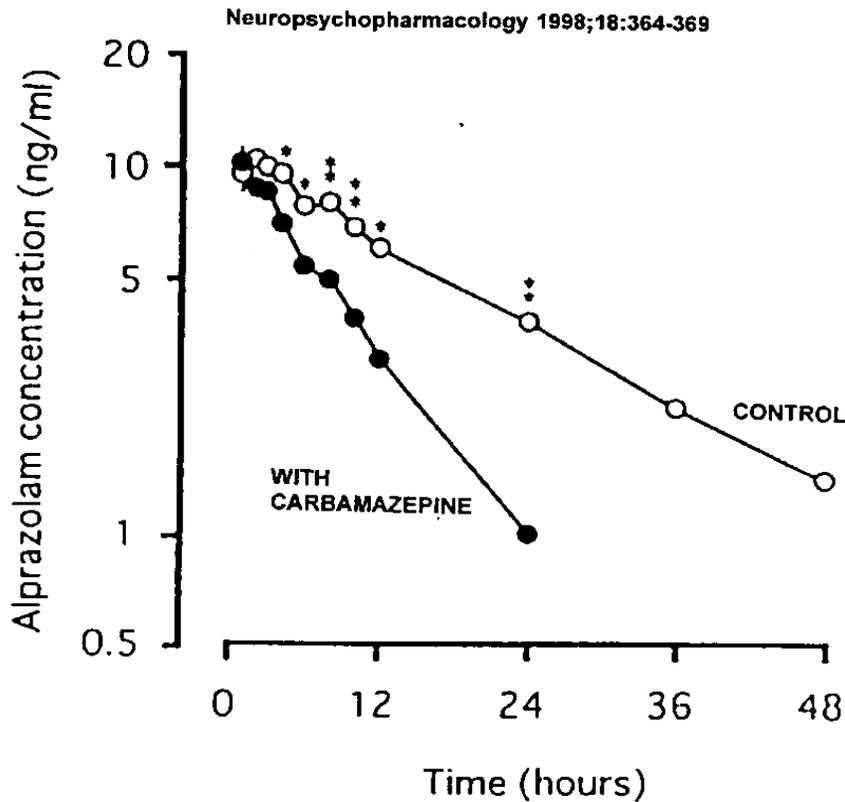


PHA 5127 Dose Optimization I

Homework II

1. A study was conducted to investigate the drug interaction between Alprazolam and Carbamazepine. The same dose of Alprazolam was given either alone or with carbamazepine by iv bolus and then concentration of Alprazolam was measured for both scenarios. Please answer the following questions. Assuming other conditions are same. (5)



(1) Please calculate the initial concentration of Alprazolam at these two scenarios based on the measured concentration shown below. Are they same? Please explain. (2.5)

Time (h)	Conc. (Alone)	Conc. (With Carbamazepine)
12	6.69 ng/ml	3.16 ng/ml
24	4.50 ng/ml	1.01 ng/ml

(2) In this study, Alprazolam was given at dose of 0.8mg. Please estimate the clearance of Alprazolam at these two scenarios. (1.5)

(3) Is Alprazolam likely to be a high or low extraction drug? Please explain. (1)

2. One patient was given two different drugs A and B by iv bolus, the given dose and measured half life are as follows: (1)

Dose (mg)	T _{1/2} (h) of Drug A	T _{1/2} (h) of Drug B
40	10	3.47
60	15	3.47
80	20	3.47

- A. B is eliminated by zero order
- B. Both A and B are eliminated by first order
- C. B is eliminated by first order
- D. Both A and B are eliminated by zero order

3. The fraction of plasma protein binding of Drug A and Drug B are 95% and 85% respectively, and both drugs bind to low affinity high capacity proteins in plasma. $T_{1/2}$ of Drug A is 4h if administered alone. If Drug A is administered together with Drug B, the $t_{1/2}$ of Drug A will be: (1) (Assuming clearance is not affected by coadministration.)

(A) < 4h; (B) > 4h; (C) >8h; (D) >9h; (E) No change;

4. TRUE (T) or FALSE (F) (3, each 0.5)

(1) If the half life of a drug is 2h, it means that from any time point it takes 2h for concentration to drop half of it.

T F

(2) When the drug which is intestine p-glycoprotein substrate is given by iv bolus, it is likely that less metabolites will be formed compared to a non-substrate drug (assuming other conditions are same).

T F

(3) If the elimination of drug follows the first order, the rate of elimination is affected by the amount of drug in the body.

T F

(4) If the drug has strong tissue binding, there must be a lot of drug accumulated in tissue.

T F

(5) When drug clearance gets smaller, then it always take longer time for body to get rid of drug.

T F

(6) Drug B, known to induce enzymes also responsible for metabolism of Drug A, will significantly affect the clearance of Drug A which is a high extraction drug if they are given together.

T F